

Knowledge and uncertainty in Lyme disease detection: an evidence-based activism research study in the UK

Article (Accepted Version)

Bloor, Kate, Hale, Vahsti and Faulkner, Alex (2020) Knowledge and uncertainty in Lyme disease detection: an evidence-based activism research study in the UK. *Critical Public Health*. pp. 1-13. ISSN 0958-1596

This version is available from Sussex Research Online: <http://sro.sussex.ac.uk/id/eprint/89516/>

This document is made available in accordance with publisher policies and may differ from the published version or from the version of record. If you wish to cite this item you are advised to consult the publisher's version. Please see the URL above for details on accessing the published version.

Copyright and reuse:

Sussex Research Online is a digital repository of the research output of the University.

Copyright and all moral rights to the version of the paper presented here belong to the individual author(s) and/or other copyright owners. To the extent reasonable and practicable, the material made available in SRO has been checked for eligibility before being made available.

Copies of full text items generally can be reproduced, displayed or performed and given to third parties in any format or medium for personal research or study, educational, or not-for-profit purposes without prior permission or charge, provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way.

The heightening crisis of Lyme disease detection: Uncertainty, knowledge, activism and politics in the UK

ABSTRACT

There are increasing levels of concern about policy and practice related to Lyme disease testing and diagnosis in the UK. A complex debate has emerged, with patient groups challenging clinical and testing practices. This paper focuses on four dimensions of diagnostic testing: accuracy, types of test, clinical application and test interpretation, to illustrate the divergence amongst and between official and patient group views. We explore these issues via analysis of information from sources including patient organisations' documents and statutory policy and professional publications, supplemented by data from an online questionnaire survey. Our analysis shows lack of consistency in policy, consumerist strategies among patients, and official policy that inhibits illness identity and maintains hard boundaries between patients' experience and public health practice. We suggest that medical policy and practice have become entrenched in defensive testing and clinical protocol. We note recently emerging trends in consultation and patient group involvement, illustrating more participative public health governance. Further, as a joint patient organisation-academic project, we contribute to understanding of patient organisation activism in public health by demonstrating our own collaborative, reflective 'evidence-based' activist research. Notably, in doing so we deploy a variety of forms of knowledge and 'evidence' beyond the often acknowledged, but limited 'experiential' and 'embodied' forms. On this basis we recommend that shared-decision-making and 'facilitational' advocacy would improve patients' empowerment and experience of testing and diagnosis. We argue that such reforms will enhance the perceived legitimacy of 'chronic' Lyme disease claims even under the conditions of scientific and medical uncertainty that prevail.

Introduction

There are few dimensions of the aetiology, epidemiology, scientific evidence base, clinical practice, service delivery, and public health policy on Lyme disease that are not disputed (Tonks, 2007). It was first described in the early 1970s (O'Connell 1995), and the bacterial infection *Borrelia burgdorferi* was identified in 1983. Infection is caused by tick bites (deer and sheep types of ticks) and is thus infection is more prevalent in rural areas though some urban areas show high rates of diagnosis. It

has become increasingly common in the UK (Dubrey et al, 2014). Symptoms are contested but might include rashes (including erythema migrans (EM) - the typical 'bull's-eye' rash) and flu-like symptoms such as headaches, high temperature, and aching joints. Later symptoms might include joint swelling, problems of the nervous system, and heart inflammation (Dubrey et al, 2014). Some symptoms may be shared with fibromyalgia or chronic fatigue syndrome, though cognitive symptoms may differentiate Lyme disease (e.g. Cairns & Godwin, 2005). Acute cases are normally treated by antibiotics. While the acute form is medically accepted, a chronic, long-term form is greatly disputed.

Diagnostic processes have been a prominent focus in studies of contested diseases (Jutel & Nettleton, 2011). Whilst we do not recap here the list of conditions with 'medically unexplained symptoms' that medical sociology has documented, we note that 'chronic' Lyme disease can appear as an 'illness you have to fight to get' (Dumit, 2006) or need 'permission' to suffer from (Nettleton, 2006). Patient group and state governance activity around Lyme disease have sharply increased over the last decade in the UK. Disease identification and testing have a particularly contentious position in these debates (Borgermans et al, 2015)., We approach these developments through related recent literatures on patient involvement and 'evidence-based' activism, critical analysis of evidence-based medicine (EBM), and emerging modes of public (health) governance.

The last three decades have seen a broad societal reconfiguration and re-legitimation of public governance of science, well-described as developing 'social robustness' through extended societal participation (Nowotny, Scott & Gibbons, 2001). Simultaneously, evidence-based medicine (EBM) and health technology assessment (HTA) have become governance movements involving massive production of clinical guidelines policy, heightening a key tension between 'algorithmic' guidance and clinical judgement (Greenhalgh, 2014). The move toward stakeholder governance involves an increasingly prominent participation of patients and patient organisations in healthcare policy and biomedical science, which has long been advocated for public health research (Popay & Williams, 1996). Many different conceptual tools have been developed to understand patient participation, but two primary foci can be discerned: first, on the types of 'engagement' that healthcare policy seeks to encourage from patients and publics, and second on activism, formulated with concepts such as 'health social movements', and 'patient advocacy organisation'.

The advance of EBM/HTA, together with emerging patient involvement and activism, have highlighted the increasing role of knowledge and ‘expertise’ in public health governance. Citizen and patient engagement in the production and deployment of knowledge has been called ‘evidence-based activism’ (Rabeharisoa, Moreira & Akrich, 2014), primarily characterised as where experiential knowledge is brought into interaction with knowledge claimed by authoritative institutions – ‘credentialed knowledge’. Most scholarship in this area emphasizes the role of ‘experiential’ knowledge (e.g. the highly cited paper (according to *Google Scholar*) by Caron-Flinterman, et al, 2005). However, as Rabeharisoa et al note, the type of credentialed knowledge that patient organisations deploy can in principle vary widely, including what others have called ‘contributory expertise’ (Collins, Evans & Weinel, 2016) in scientific biomedicine itself, and forms of healthcare evaluation akin to health technology assessment. A detailed focus on knowledge developed by patients specifically related to disease tests also has been elaborated, especially in the context of the vagaries of multiple, technologically differing tests around a given condition (Corbett, 2009).

Against this background, the aim of this paper is conceptual, analytic and policy-oriented, exploring the dynamics of contested positions and reflecting on the knowledge practices that are deployed, including by ourselves. By analysing recent official and professional guidance on clinical pathways for disease testing, assessing its coherence, comparing it to patient groups’ positions, by referring to scientific publications, and by giving examples of patients’ views relevant to policy we aim to show the possibility for reforms to policy and medical practice. Further, we use the Lyme disease (LD) case to enhance understanding of contemporary public health governance-related knowledge practices. In particular, while experiential knowledge is acknowledged as important to patient group activism, we aim to make a distinctive contribution by extending this widespread depiction (e.g. Staley and Doherty, 2016; Caron-Flinterman et al, 2005) by referring to and illustrating in our own collaborative methodology a variety of other types of activist research-based forms of knowledge that are frequently overlooked.

Our primary analysis, of policy discrepancies and patient group positions, is structured around four dimensions of testing: 1. Accuracy; 2. Types of test; 3. Clinical application; and 4. Interpretation of test results. On the basis of our multidimensional, multi-method analysis, we argue that official policy and clinical practice inhibits patient empowerment, autonomy and illness identity, maintains hard boundaries between patients’ experience and the public health community, encourages a

‘consumerist’ pro-choice approach to testing among patients, and upholds an inconsistent and potentially restrictive definition of Lyme disease.

Methodology

The primary methodology employed was content analysis of patient groups’ online documents and websites, and official national policy statements and documents. While we focus on their textual content, we do so recognising that documents have a performative, active function in policy-related networks as part of ‘an entire complex of events’, ‘entering into the stream of interaction’ (Prior, 2008). A wide range of recent and current literatures within public health, infectious diseases, and medical science and social science literature was also identified and drawn upon. We searched Google Scholar from early 2016 to February 2017, and some important documents were part of an ongoing monitoring collection conducted by information/activist group Lyme Research UK (Author KB). (A chronological list of the main policy and patient group sources is provided separately online (Supplementary material)). Some patient groups’ online statements are frequently revised, and we have used these published sources rather than direct observation or interviews, but our analysis was current at the time of writing.

We developed a systematic, comparative approach to documentary analysis (Bowen, 2009), identifying patterns of discourse in the selected sets of material. These documents were examined to derive themes, subthemes and relevant statements. Two of the authors (KB and VH) repeatedly cross-compared the key topics, themes and significant extracts to enhance validity of the selections and analysis. Taking into account the large number of UK Lyme patient groups, we focused in most detail on the two most prominent, selected on the basis of volume of online material, membership, and having strong links with patients: Lyme Disease Action (LDA), and Lyme Disease UK (LDUK). Centrally, we undertook what we term a ‘method of discrepancies’ form of content analysis, identifying detailed differences between official organisations’ statements, and between official organisations’ and patient organisations’ statements, guidance and claims, by systematic cross-comparisons. There is precedence for such a method as a ‘policy audit tool’ (albeit on a larger scale) in public health policy research (e.g. Kohl et al, 2012).

We supplemented these secondary sources, with primary data from an online survey conducted in 2011 by Lyme Research UK (LRUK, author KB) of patients who had a diagnosis of LD made in the UK. Potential participants were approached online (mainly Facebook groups), on the website of LRUK, and by contact to over a hundred organisations and high-risk groups (e.g. veterinary occupation, hill walkers, etc) directly and via support networks. One hundred and fifty-two completed an online questionnaire, being self-selected and thus probably skewed toward people with particular concerns about Lyme disease. Professional ethics guidance from the Social Research Association (UK) was obtained. (Reports of the survey are available on the website of LRUK (<https://lymeresearchuk.org/links/>)). The survey invited participants to provide free text comments on their experiences on testing, diagnosis and treatment. About two-thirds of people provided comments. We searched these free text comments for explicit references to the broader testing regime: the NHS, policy statements and guidelines, and policy institutions such as the (then) Health Protection Authority and the national reference laboratory (RIPL) for infectious disease investigations. The selection was made using keyword text searching and repeated re-reading by author KB and then checked and a second sub-selection made by author AF.

It is important to our aim in the paper of demonstrating different forms of knowledge that can be mobilised in disease activism to note that our method is a collaboration, combining academia-based and patient organisation-based researchers (LRUK). We can describe our collaboration as ‘evidence-based activism’, which as Rabeharisoa et al have surmised in the case of Attention Deficit Hyperactivity Disorder (ADHD), can take the form of a ‘joint epistemic and policy enterprise’ (2014: 121). Our methodology thus exemplifies the alliance-building noted as a feature of certain patient organisation strategies (Rabeharisoa, 2003). Our own form of research-based activism can be located in a spectrum ranging from public political demonstration on one hand, to close engagement with and critique of scientific and policy positions on the other (the current project/paper being at the latter end of the spectrum). Given that our collaborative project is itself a topic, as well as resource, of this paper, we give a brief outline of its origin and methods of working.

Community group LRUK works in various ways - by directly interacting with agencies such as medicines regulators, Public Health England and the National Institute for Health and Care Excellence (NICE), by interacting through online (e.g. Facebook) groups, and by forming collaborations with academics, including clinical academics and, as in the present collaboration,

social science/medical sociology. LRUk aims to clarify and improve medical practices and policy regarding Lyme disease, and aims for formal academic credibility for its research-based agenda. Equally, academic-based medical sociology author AF has personal and professional concerns about disputed medical conditions and in particular the fragility and contestability of diagnostic test results. A collaboration was formed on this basis. The role of author AF was regarded as ‘facilitating’, and that of author KB (LRUK) as mediating patient/patient groups’ perspectives and providing a wide range of informational materials built up over more than 10 years. Author VH is an associate of LRUk and acted primarily as a policy document analyst. These roles were not clear-cut, for example, author KB conducted literature searches for academic papers on diagnostic uncertainty and infection science. The project, unfunded, is seen as a learning process on each side, developed through face to face and tele-meetings and email exchange. Through the present paper, therefore, the shared aims of the collaboration were to highlight the apparent growing concern about Lyme disease evident in the public domain, to demonstrate an academically credible understanding of the policy and patient group dynamics involved, and to present an analysis of public policy and patient groups’ activism that shows the wide range of different knowledges that they/we draw on and which could underlie constructive proposals for improvement. In order to achieve such credibility, normal academic social science standards of data selection, justification and interpretation have been employed.

Lyme disease testing standards in the U.S. and U.K.

Here, we outline the forms of Lyme disease tests, and criticisms that they evoked initially. This now standard testing approach can be traced to the ‘Dearborn’ conference in the USA (ASTPHLD, 1994; the Second International Conference on Serologic Diagnosis of Lyme Disease). Specific approaches to ‘two-tier’ antibody blood testing were endorsed as standards at this conference. The method involved a first stage ‘ELISA’ (‘enzyme-linked immunosorbent assay’) test, which, if ‘positive or equivocal’, was followed by a ‘Western blot’ (WB), a visually interpreted test for specific antibody patterns. These tests for specific antigens aimed to indicate past or current exposure to the bacteria. In cases of a chronic condition, positive Western blot results could be interpreted clinically as negative for Lyme disease under this algorithm. (Expanded on in the ‘Application, symptom definition and interpretation of tests’ section below). There were many criticisms in the US at the time. Two professional groups took contrasting positions (Tonks, 2007), not detailed here, and

patient movements were seen by public health professionals to exert inappropriate influence (e.g. Auwaerter et al, 2011). These controversies are echoed by recent UK developments.

In the UK in 2015, Lyme disease received greatly increased media attention when a prominent high-street business owner, John Caudwell, reported that the disease had been contracted by his family, founding the Caudwell LymeCo charity, calling for more research and challenging existing policy (Independent, 2015; Caudwell LymeCo, 2019). Patient groups have proliferated. Lyme Disease Action (LDA) was set up in 2004, and smaller mostly unfunded community groups or charities developed, such as Vector-borne Infection Research Analysis Strategy (VIRAS), in 2016; Lyme Disease UK (LDUK) in 2014; Lyme Research UK (LRUK) in 2011; LymeAid in 2014, About Time for Lyme in 2015, and Fight Lyme Now. These groups have somewhat different emphases, agendas, knowledge practices, and relationships to policy forums.

The current UK (England) statutory sector position has been led by Public Health England (PHE) from 2012 (formerly Health Protection Authority - HPA), and its reference laboratory for testing - the Rare and Imported Pathogens Laboratory (RIPL). A range of knowledge-intensive governance developments have appeared recently. NICE placed additional information on LD online in 2014, and in 2016 began formal guidelines development, including consultations with interested parties. A discussion was held at the House of Lords in October 2015, and the UK Department of Health began reviews in 2016 including a systematic review of evidence including professional and patients' experience of diagnosis (EPPI Centre, 2017). The British Infection Association (BIA), the primary professional body for infectious disease, had published a position statement somewhat earlier (BIA, 2011). The official organisations base their positions on extensive reviews of scientific research, typically following 'systematic review' methods (NICE), or drawing 'on the experience of UK infectious diseases physicians and medical microbiologists...(taking) full account of extant national and specialist societies' guidelines', and with 'full involvement of the BIA membership through a consultation process' (BIA, 2011). Issues of testing remain at the centre of these developments.

Findings

In the following three sections we present our document analysis and interpretations, combining first the twin issues of types of tests and their accuracy, and second the symptom-based application

of tests and their interpretation. We show official/statutory organisations' positions, and the usually contrasting positions of patient organisations. This is followed by survey-based illustrative examples of patients' knowledgeable, experience-informed views on standard testing practices in the context of NHS organisational structures.

Types of tests and the accuracy of the NHS 'statutory' tests

Public Health England's crucial 'Suggested Referral Pathway' (PHE, 2014a) is a short guideline document. It refers to potential inaccuracy of NHS standard Lyme tests only for very specific, early stage circumstances. When a bull's-eye rash is present, testing is not advised because 'an antibody response to Lyme can take time to develop', and the BIA also recommends that the test should be taken 4-6 weeks after infection (2011: 5). While the then HPA also stated that the 'heterogeneity of *Borrelia* makes the selection of antigens for immunological testing difficult' (2012:13), the PHE referral pathway guideline does not mention this issue. Overall, poor test performance is not highlighted in official documents.

The PHE referral pathway also refers to the effect of immune-suppressant drugs, and prior treatment with 'inadequate' antibiotics potentially causing false negatives (PHE 2015:2), but this is not mentioned in detailed advice on the PHE website, nor 'Lyme Services at the HPA' (2012), nor NICE (2015) or the BIA guidance (2011). If a patient still registers a positive test after 2 or 3 weeks of antibiotic treatment, even if they still have symptoms, this is termed 'post Lyme treatment' syndrome (HPA, 2012:11). Likewise, BIA states that 'seropositivity persists indefinitely in some patients' (BIA, 2011: 5). However, notably, some LD test manufacturers' instructions for test kits for the Western Blot (used by the NHS) do state that early therapy can invalidate the test result (e.g. Viramed Biotech AG, 2015: 4). However, this is unlikely to be read by first line clinicians.

Patient groups LDUK, LDA and Caudwell LymeCo have all questioned the overall reliability of the NHS 2-tier tests. LDUK highlight research that suggests 'a sensitivity of around 50% which means that approximately half the tests carried out could result in false negatives' (LDUK, 2016, website), while Lyme Research UK suggested that after several weeks of infection the sensitivity can be as low as 44% (2011;2016), so test timing could lead to treatment delays (Caudwell LymeCo, website, August 2018). LDA states that no current test can 'confidently rule out Lyme disease' or 'confirm...active

disease' (LDA, 2017). Whether tests recognise specific strains of *Borrelia* is also questioned (VIRAS 2017:3, Lyme Research UK, 2016: 91), and it is further suggested that the data sets for assessing the validity of test kits were determined in patients with known or probable borreliosis, leading to a biased range of clinical indications (VIRAS, 2016: 127). (Such a comment would not be out of place in an official health technology assessment analysis of evidence bias). Many patient groups comment that clinicians should diagnose more clinically, rather than having recourse to dubious tests, to give patients more chance of treatment.

There are a wide range of different non-mandated types of tests available, mainly offered by private clinics. Some tests are not based on detecting antibodies but on other immune responses, and some use 'direct' methods, such as PCR (polymerase chain reaction) to identify the DNA of bacteria. Blood or tissue can also be examined using microscopy. A report in 2006 for the Department of Health reviewed many of the different types of testing, concluding that many were unorthodox and unvalidated (Duerden, 2006). NICE recently supported the 2-tier method (NICE, 2015), and the PHE referral guidance advises that with patients who test positive from 'non-NHS laboratories', clinicians should repeat or provide NHS testing, and seek advice from infectious disease authority RIPL on accreditation status (PHE, 2014a:2); other tests are possibly to be offered to identify non-LD potential factors (2014a: 2). A PHE leaflet for the public mentions that other tests for tick borne infections are available, but otherwise reflects the PHE's cautious position (PHE, 2015: 4). Professional body the BIA mentions culture testing, which is described as 'difficult to standardise' and PCR tests that might be considered in 'certain well-defined circumstances' (BIA, 2011: 331). RIPL include an option for a PCR test on their test request form for GPs, and an FOI request to RIPL (by author KB/LRUK) revealed that tests carried out by RIPL in the UK with 'Lyme disease PCR' have risen from zero in 2012 to nearly 200 by 2016 (FOI, 2017). Overall, we see that several different policy guidances reinforce the 2-tier, non-chronic testing regime.

A range of test kits was considered in NICE's consultation on guideline development (author KB's fieldnotes, June 2016) including novel approaches such as for pathogen detection (e.g. membrane proteins enrichment and spectroscopy). Informed UK Lyme patient groups proposed a variety of other tests during this consultation such as fluorescence in situ DNA hybridization, and microscopy using digital filters and pattern recognition (NICE, 2016:94). LDUK show consideration of a broader range of tests overall and include a small number of these on their website

(<https://lymediseaseuk.com/>, August 2018), without endorsing any particular type. It 'strives to highlight all available, known options' including private tests, noting accreditation status for the laboratories. On the other hand, LDA express concern about certain tests which they consider may not have a solid evidence base, and that 'independent' or 'unorthodox' testing might be disregarded by the NHS, hence provoking expensive private treatment (LDA, 2017). Patients may view private clinics and labs to be 'accredited' regardless of whether PHE/RIPL regards them as such and many UK patients do travel abroad to undergo tests, often associated with specific private laboratories. From the LRUUK survey in 2011 of 152 patients, 46% had had one or more tests in non-UK laboratories (Lyme Research UK, 2011), showing the deep divergence from official policy of patients' help-seeking practices.

In summary, official guidance is not wholly consistent, and the uncertainty of the 2-tier test is a central concern for many patient groups, advocating that this should be taken into account during diagnosis and better communicated with patients. Patients are positioned as passive recipients of these tests. Patient groups' calls for greater emphasis on the clinical encounter points to the more empowered role that many would prefer. Patient groups have been proactive in researching other tests, many wishing a wider range to be accepted, in other words a more consumerist principle of 'choice'. Tension is caused by NHS doctors disregarding 'unorthodox' tests, so disallowing possible choice and hence, patient autonomy. The range of non-endorsed tests constitutes a confusing diagnostic environment.

Application, symptom definition and interpretation of tests

Patients' experience of Lyme disease testing and diagnosis is also shaped by policy on symptom definition for application of tests, and embedded guidance on test interpretation. Policy documents in the UK display significant differences between each other on indicative symptoms for testing. These include the importance of the EM 'bull's-eye' rash as an early-stage indication. For example, PHE recommends that antibiotics should be given if the patient presents with an EM rash (2014b), and if there is no rash but there are symptoms 'suggestive' of LD and with a 'credible risk of tick exposure', a test should be taken (PHE 2014a: 1), a degree of discretion that leaves the decision to the vagaries of individual clinical judgment. However, the BIA guidance goes further: use of standard 'IgM' tests should be reserved for patients who have *acute* symptoms and with a high probability of Lyme borreliosis, and laboratories must receive clinical details including dates of illness onset and

most recent tick exposure (BIA, 2011: 333). Only NICE (2015) mentions the possibility of secondary, later-stage rash. Patient UK and a PHE leaflet (n.d.) for GPs mention the possibility that primary rashes may be absent, though only in relation to specific symptoms such as neuropathy or arthralgia (joint pain). Taken over the range of official sources such as the PHE GP guidance and public-facing NHS Choices (2015), nonspecific symptoms such as arthritis, joint pain, and associated swelling are inconsistently identified as possible indicators. Thus, there is significant ambiguity in and between these different symptom guidances.

Alongside the above inconsistencies, official sources omit many symptoms considered important by patient groups. Fatigue in particular is rarely mentioned, and ‘chronic fatigue’ is completely absent. Nor is there mention of psychological, mood/emotional, or psychiatric symptoms (though the nonofficial Patient UK website lists confusion, memory and concentration impairment, mood changes in schizophrenia-like illness for late stage Lyme). Many Lyme patient groups’ documents state that diagnosis should be more clinically based on symptomatology and history, lab tests being only a secondary measure, supported in observation of groups’ participation in the NICE guideline scoping process (author KB fieldnote, 2016).

Test methods are complex, containing human or automated elements. The U.S. Center for Disease Control and Surveillance (CDC, authoritative and somewhat equivalent to England’s PHE) usefully describes the standard Western Blot test as comprising: ‘...several lines or “bands”. Each line represents antibodies to a different component of the bacteria.... it is the combination of multiple, specific lines that identifies the infection as being due to *Borrelia burgdorferi*’ (CDC, 2015), warning that it is incorrect to ‘interpret a test result that has only some bands that are positive as being ‘mildly’ or ‘somewhat’ positive for Lyme disease’ (CDC, 2015), concluding that ‘If this sounds complex, it’s because it is’. This technical complexity clearly adds to the overall uncertainties described above, both for clinicians and for patients.

Recommended test interpretations are opposed by some patient groups as too restrictive. We point to scientific studies not included in official narratives, which continue to propose variations on how the tests should be defined and which antigens should be identified for a positive result (e.g. Goettner et al. 2005). Variations between manufacturers’ instructions and official policy on interpretation shows that instructions are sometimes ambiguous. For example, a Western blot test

manufacturer's statement that 'A final clinical diagnosis should always be made considering anamnesis (i.e. patient's recollection), clinical manifestations, and laboratory data' (Viramed® Biotech AG 2015: 3), suggests enhanced scope for clinical discretion. Opposing the BIA position, 'persistent seropositivity' is promoted by Lyme activist groups and patients.

In summary, inconsistencies in symptoms described in official documents makes diagnosis and identification of patients for testing uncertain, making access or non-access to tests insecure. In general, patient groups argue for a much wider range of symptoms to define the disease than the official testing and diagnostic regime allows. It follows that patient groups believe there is a high level of under-diagnosis and denial of chronic infection. Official test interpretations are heavily and *knowledgeably* criticised, including drawing on emerging science to challenge prevailing antigen interpretations. The technician discourse of the public health bodies acts as 'boundary-work' (Gieryn, 1999), discouraging communication between health professionals and lay public or patients, and representing an 'algorithmic' approach to evidence-based medicine (Greenhalgh, 2014).

Patients' knowledge and views of the policy environment

In order to illustrate people's perceptions of the Lyme disease policy environment, we provide in this section a short selection of free text comments made by respondents to the LRUk online survey (see Methods). We do not attempt a comprehensive analysis, but illustrative examples of their experience-based knowledge, technical insight, and views, related to national policy and organisational actors. ('HPA' below refers to the national then Health Protection Authority, now superseded by Public Health England).

This participant comments on their local NHS clinical specialists, seeing institutionalised bias:

The local (city) infectious disease consultants are vehemently opposed to chronic tick-borne infection... am shocked at the strong entrenched views of local specialists who inform the local GP's of their dogma. (SR (survey respondent) 25, negative NHS test results, age group 56-65, male (retired doctor)).

This patient shows a knowledgeable level of understanding of test performance and refers to national policy guidance:

... GPs should have more training in interpreting the results. They do not appear to understand the timing issues nor that the test may be a false negative... Why does it appear that no-one within the NHS with any power to change things wants to help us to understand the condition? ... A condition management nurse and physiotherapist locally have been amazing but their suggestions have been 'poo- pooed' by consultants... Is this to do with the HPA guidelines? (SR 40, negative NHS test results, age group 46-55, female).

The internal communication pathways of the NHS were referred to by several survey participants, and here a test manufacturers' technical user instructions are also understood by the patient, pointing to discrepancies between the two:

GPs are not informed by HPA (reference laboratory) of potential reasons for a negative ELISA test, or the option of further tests for other illnesses - as recommended on Trinity Biotech's ELISA leaflet. Information is being held back by the lab. (SR 82, negative NHS test result, age group 46-55, gender not known.)

and:

The NHS is very willing in my experience but is hamstrung by the views promulgated by the [reference laboratory]. (SR 102, positive NHS test, age group 65+, female).

Finally, this example illustrates a patient's knowledge of official policy of the national reference laboratory on (the disputed) appropriate treatment:

Fortunately (I) have a very good GP. He's taken time to learn about the condition... All other experiences with NHS very poor...(private) treatment stopped too early, against my wishes and relapsed. I think this happened due to the 'pressure' originating from the HPA guidelines criticising long term antibiotic treatment. (SR 109, negative NHS test result, age group 46-55, male).

Patients providing comments in the LRUUK survey were self-selected, and the majority of comments overall described personal experiences. Given the context of the survey, the comments can be expected to be critical, and very few positive comments could be found. A perception of institutionalised medical power and protocols is very evident. Clearly, these comments echo some of the activist patient groups' positions set against the official policies analysed above, as well as showing a variety of technical and organisational, as well as 'experiential' knowledge.

Discussion and conclusion

Official policy has described Lyme disease as a 'convenient container' for a wide array of symptoms (HPA, 2012: 23). An influential report warned against 'unreliable' tests, non-uniqueness of later stage symptoms, and 'fringe practitioners' diagnosing Lyme disease (Duerden, 2006), when conditions such as motor neurone disease or Addison's disease were in fact present (HPA, 2014). The perpetuation of this position from at least the mid-2000's to date suggests an entrenched position, which our analysis has illuminated. We have illustrated the extreme uncertainties in defining types and symptoms of the disease, a proliferation of non-NHS test technologies generally disputed by NHS and public health guidelines, and conflicts over the accuracy and appropriate interpretation of the standard testing regime.

The controversies over the scientific basis of tests and the relative importance of clinical diagnosis highlight the alleged 'crisis' of evidence-based medicine (Greenhalgh, 2014). The entrenched positions may be explained partly as a reaction to high diagnostic uncertainty. Medical practitioners' reliance on standardised algorithms, and 'rituals' has been widely noted in medical sociology (Atkinson, 1995; Berg, 1998) and this may account for some of the embedded routines reported. A cautious, conservative NHS policy on new diagnostic tests in general is unsurprising (Hofmann and Welch, 2017). In Lyme disease, dismissive policies have denied patients a medicalised 'illness identity' (Conrad and Barker, 2010) which may afford existential security and self-empowerment, regardless of therapeutic possibilities.

The differences between patient organisations are important in understanding Lyme disease activism, and their positions are sometimes revised (as with Caudwell LymeCo moving to a more tentative position regarding private testing). We note that our analysis shows varying positions on diagnostic testing. We have shown how some recommend particular tests on the basis of quoted evidence, while others more cautiously point to the NHS's position on non-standard testing. Some engage more closely than others with the scientific evidence, such as symptomatology. Most, though not all, groups have little funding. They can be characterised, crudely and oversimplifying, by their key modus operandi. One is well resourced and connects closely with clinicians, scientists and policy networks, organising conferences (LDA); one is more focused on direct patient support, has

promoted surveys of patient experiences, and links to less established, critical science (LDUK); one is small, relatively autonomous, and highly engaged with detailed scientific debate (VIRAS); some are focused on awareness-raising and do not engage directly with scientific evidence (e.g. About Time for Lyme; this group partners with Vis-a-Vis Symposiums, which convenes awareness meetings with clinicians as well as the public: <https://www.abouttimeforlyme.com/the-project>). Thus, some groups are more overtly critical and adversarial than others, drawing on somewhat different knowledge bases and taking varied and sometimes overlapping stances on testing, and in their organisational relation to scientific and public health authorities.

Considering the different types of knowledge or expertise highlighted in scholarship on the patient voice in health policy and in patient organisations' involvement or activism, we have emphasized the need to analyse modes of knowledge beyond the experiential. The concept of 'evidence-based activism' (Rabeharisoa et al, 2014) is useful in that it draws together the two notions of activism and knowledge, and it raises the question of what types of evidence or knowledge are being produced and mobilised. The range of types of expertise that patient organisations or patient-academic collaborations display, has not been well conceptualised in recent scholarship, with some partial exceptions (Orsini & Smith, 2010). With our data and analysis, therefore, we contribute to this field by illustrating a diverse range of different types of and relationships to knowledge that different Lyme disease patient organisations mobilise, and also that we, as a patient organisation-academic collaboration, have produced. Both LDUK and LDA can be seen as 'evidence-based activist' organisations, with LDUK in particular meeting all the criteria of: experiential knowledge, articulation of credentialed knowledge, redefining the disease, and participating in established networks of expertise (Rabeharisoa et al, 2014). In our own collaborative evidence-based activism and research, we have brought together and deployed a hybrid mixture of knowledge including de novo policy analysis, policy audit, 'experiential' patient knowledge and perspectives on the LD policy environment (gathered through online survey), investigative inquiries (e.g. FoI requests), content analysis of patient group positions and publications, participant observation of (NICE) meetings, 'technical' understanding of test technologies, and critical review of scientific evidence.. The research presented here therefore represents a form of activism that shows a wide multidimensional range of research-based evidence production, which goes well beyond the 'experiential' knowledge typically attributed to patients and patient groups.

Our research collaboration provides the basis for a number of suggestions for clinical practice and public policy. Notably and most obviously, given our ‘method of discrepancies’, the various diverging official policy statements and guidance could and should be made more consistent. We offer three further suggestions.

First, efforts can be made to mitigate the confusion caused by the proliferation of test technologies. NICE collected information on 34 test kits in its review, a positive step, even though most non-mandated tests were discounted on grounds of weaknesses in evidence, and the full list of tests was not placed in the public domain. The extent to which different tests can currently be compared is slight, so further research into tests deemed of higher likely validity could be undertaken. Nevertheless, we point to recent innovations that appear promising (e.g. Mavin et al, 2014), and we note for example a ‘credentialed’ development of scientific evidence about the conversion of microbial infections into chronic conditions, including in Lyme disease (O’Connor et al, 2006). Patient group knowledge-based involvement, whether activist or elicited, can have a role in highlighting such emerging research in public health forums, including such as an academic journal.

Second, conspicuously absent from our data is the widely advocated paradigm of patient-centric *shared decision-making*. This paradigm emerged from the advance of Evidence-based Medicine, acknowledging that the knowledge enshrined in evidence-bases is often uncertain, and that this uncertainty can be ethically shared with patients. There is definite scope for exploring this approach, complex though it may be (Stiggelbout et al, 2012), including in decisions about the role of testing. Alternative tests might be presented to patients as part of clinical discussion, even if not recommended, which would align with the health service’s own ‘empowerment’ and ‘choice’ agendas around citizens’ rights. This would address patients’ consumerist orientation to tests. Central to such an approach would be to acknowledge the complexity and uncertainties of testing and diagnosis in the context of chronic symptoms, and to acknowledge the technical knowledge of testing that many patients evidently develop. Such an approach would counter the recourse to ‘algorithmic’ EBM and acknowledge the EBM movement as constituted by particular, selective kinds of knowledge and epistemology (Lambert, 2006). Thus, shared decision-making could alleviate to some extent the ‘embodied doubt’ (Nettleton, 2006) experienced by patients, and lend greater legitimacy to illness experiences and identities than questionable tests and test results alone can.

Third, we witness currently an increase in public health advocacy, and some infectious disease specialists are sympathetic to a broader if selective definition of Lyme disease. Thus, there is opportunity to further official policy development. In this light, we note the partial acceptance of a recent suggestion from a U.S.-based international 'ad hoc committee' including human rights lawyers and public health physicians, that World Health Organization (WHO) International Classification of Disease (ICD) codes covering LD should be revised on humanitarian grounds (Ad hoc Committee, 2017). Such advocacy could draw on 'contributory rights' (Collins et al, 2016), and take a community-focused 'facilitational' form, rather than an 'elitist' broadcasting form (Smith and Stewart, 2017).

In this vein, an internationally-authored editorial in the *British Medical Journal* (Borgerman et al, 2015) is significant in arguing for a broader debate including patient groups amongst the 'stakeholders'. This multi-actor 'engagement' language of 'stakeholders' signals a re-orientation of the modes and scope of policy governance in Lyme disease, echoing wider trends. We see, therefore, a reconfiguration of the accepted institutional grounds of 'credentialed' knowledge (Rabeharisoa et al, 2014), even if the officially claimed knowledge itself remains little disturbed. The initiatives of NICE and Department of Health (EPPI Centre, 2017) may be understood as moving in this direction, though our analysis suggests there is scope for further responsiveness and collaboration with patient organisations. Finally, our own performative activism mobilising multiple research-based as well as experiential knowledge, represented in this academic paper, can be seen as a collaborative, multi-stakeholder intervention in the field. Such actions, with suitable audience and impact, can help address the struggles of legitimacy that patient organisations and individual citizens experience in chronic Lyme disease.

References

- Ad hoc Committee for Health Equity in ICD11 Borreliosis codes (2017). At: <https://botaborrelia.wordpress.com/2017/06/28/bota-borrelia-cure-lyme-pressrelease-from-adhoc-committee-for-health-equity-in-icd11-borreliosis-codes-and-global-rbcc/>. Accessed 1.12.2017.
- ASTPHLD (1994). Proceedings of the Second International Conference on Serologic Diagnosis of Lyme Disease. (The 'Dearborn conference'). Available at: http://www.actionlyme.org/DEARBORN_PDF.pdf.

Accessed 19.6.2017.

Atkinson, P. (1995). *Medical Talk and Medical Work: the liturgy of the clinic*. London, Sage.

Auwaerter, P. G., Bakken, J. S., Dattwyler, R. J., Dumler, J. S., Halperin, J. J., McSweeney, E., et al (2011). Scientific evidence and best patient care practices should guide the ethics of Lyme disease activism. *Journal of Medical Ethics* 37(2), 68–73.

Berg, M. (1998). Order(s) and Disorder(s): Of protocols and medical practices. In: Berg M, Mol A-M (1998) *Differences in Medicine: Unraveling practices, techniques and bodies*. Durham Duke University Press, pp. 227-246.

Bowen, A.G. (2009). Document Analysis as a Qualitative Research Method. *Quality Research Journal*, 9(2), 27–40.

Borgermans, L., Perronne, C., Balicer, R., Polasek, O., & Obsomer, V. (2015). Lyme disease: time for a new approach? *British Medical Journal* 6520(December), h6520.

BIA - British Infection Association. (2011). The epidemiology, prevention, investigation and treatment of Lyme borreliosis in United Kingdom patients: A position statement by the British Infection Association. *The Journal of Infection* 62(5), 329–38.

CDC (2015). Understanding the Immunoblot Test.

<https://www.cdc.gov/lyme/diagnostesting/labtest/twostep/westernblot/index.html>, Accessed 29.11.2017.

Cairns, V., & Godwin, J. (2005). Post-Lyme Borreliosis Syndrome: a Meta-analysis of Reported Symptoms. *International Journal of Epidemiology* 34(6), 1340–5.

Caron-Flinterman, J.F., Broerse, J.E.W., Bunders, J.F.G. (2005). The experiential knowledge of patients: a new resource for biomedical research? *Social Science & Medicine*, 60(11): 2575-2584.

Caudwell LymeCo, website, <https://caudwelllyme.com/>. Accessed 2/2/17.

Caudwell LymeCo (2016) Report on submission to NICE consultation. <https://caudwelllyme.com/>

Caudwell LymeCo (2019). <https://caudwelllyme.com/why-donate-to-caudwell-lymecol>. Accessed 26/3/19

Collins, H., Evans, R., & Weinel, M. (2016). Expertise Revisited, part II: Contributory expertise. *Studies in History and Philosophy of Science Part A* 56, 103-110

Conrad, P., & Barker, K.K. (2010). The social construction of illness: key insights and policy challenges. *Journal of Health and Social Behavior* 51(S), S67–S79.

Corbett, K. P. (2009). “You’ve Got it, You May Have it, You Haven’t Got it”: Multiplicity, Heterogeneity, and the Unintended Consequences of HIV-related Tests. *Science, Technology, & Human Values*, 34(1), 102–125. <https://doi.org/10.1177/0162243907310376>

Duerden, B. (2006). Unorthodox and Unvalidated Laboratory Tests in the Diagnosis of Lyme Borreliosis and in Relation to Medically Unexplained Symptoms. Available at: https://webarchive.nationalarchives.gov.uk/20080205204935/http://www.dh.gov.uk/en/Publicationandstatistics/Freedomofinformationpublicationscheme/feedback/FOIreleases/DH_4138916

Dubrey, S. W., Bhatia, A., Woodham, S., & Rakowicz, W. (2014). Lyme disease in the United Kingdom. *Postgraduate Medical Journal* 90(1059), 33–42. doi:10.1136/postgradmedj-2012-131522

Dumit, J. (2006). Illnesses you have to fight to get: Facts as forces in uncertain, emergent illnesses. *Social Science and Medicine* 62, 577–590.

Engstrom, S. M., Shoop, E., & Johnson, R. C. (1995). Immunoblot interpretation criteria for serodiagnosis of early Lyme disease. *Journal of Clinical Microbiology* 33(2), 419–427.

EPPI Centre (2017). Prevalence, diagnosis, treatment and prevention of Lyme disease: an evidence

map and four systematic reviews. At: <http://epi.ioe.ac.uk/cms/Default.aspx?tabid=3701> Accessed 20.12.2017.

FOI Freedom of information request (2017). Rare and Imported Pathogens Laboratory PHE, ref no 18/71h289.

Gieryn, T.F. (1999). *Cultural boundaries of science: credibility on the line*. University of Chicago Press.

Goettner, G., Schulte-Spechtel, U., Hillermann, R., Liegl, G., Wilske, B., & Fingerle, V. (2005). Improvement of Lyme borreliosis serodiagnosis by a newly developed recombinant immunoglobulin G (IgG) and IgM line immunoblot assay and addition of VlsE and DbpA homologues. *Journal of Clinical Microbiology* 43(8), 3602–9.

Greenhalgh T. (2014) Evidence-based medicine: a movement in crisis? *British Medical Journal* 48, g3725.

HPA - Health Protection Agency (2012) Lyme Services at the HPA. Available at: http://www.hse.gov.uk/aboutus/meetings/committees/acdp/161012/acdp_99_p62.pdf

HPA – Health Protection Agency (2014). Unorthodox Clinical and Laboratory Practices Related to Lyme borreliosis. Available at: <http://webarchive.nationalarchives.gov.uk/20140714100737/http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/LymeDisease/LymeDiseaseDiagnosticServices/lym030UnorthodoxPractices/>

Hofmann, B., & Gilbert Welch, H. (2017) New diagnostic tests: more harm than good. *British Medical Journal* 358 doi: <https://doi.org/10.1136/bmj.j3314>

Independent (2015). <http://www.independent.co.uk/news/people/john-caudwell-phones-4ufounder-calls-on-government-to-research-lyme-disease-a6672826.html> Accessed 3/2/2017

Jutel, A., & Nettleton, S. (2011). Towards a sociology of diagnosis: Reflections and opportunities. *Social Science & Medicine*, 73(6): 793-800.

Kohl, H.W., Craig, C.L., Lambert, E.V., Shigeru, I., Alkandari, J.R., Leetongin, G., Kahlmeier, S., for the Lancet Physical Activity Series Working Group (2012). The pandemic of physical inactivity: global action for public health. *Lancet* 380(9838), 294-305.

LDA (2013). Lyme Neuroborreliosis. At: <http://www.lymediseaseaction.org.uk/latest-news/lymeneuroborreliosis-booklet/>. Accessed 2/2/2017

LDA (2017). <https://www.lymediseaseaction.org.uk/about-lyme/tests/>. Accessed 2/2/17. (website now revised)

Lambert, H. (2006). Accounting for EBM: notions of evidence in medicine. *Social Science & Medicine* 62(11): 2633-45.

Lyme Disease UK (2016). Report of submission to NICE consultation, at: <http://lymediseaseuk.com/wp-content/uploads/2017/11/LDUKs-comments-on-the-NICE-Guideline-Lyme-disease-2017.pdf> . Accessed 20.12.2017.

Lyme Research UK (2016). Submissions to NICE consultation. At: <https://www.nice.org.uk/guidance/gidng10007/documents/consultation-comments-and-responses>. Accessed 21.12.2017.

Lyme Research UK (2011) <https://lymeresearchuk.org/testing-for-borrelia/>. Accessed 2/2/17.

Mavin, S., Watson, E. J., & Evans, R. (2014). Laboratory diagnosis of Lyme borreliosis in Scottish patients: a novel approach. *British Journal of Biomedical Science* 71(2), 51–4.

Nettleton, S. (2006). 'I just want permission to be ill': Towards a sociology of medically unexplained symptoms. *Social Science and Medicine* 62(5), 167-1178.

NHS Choices (2015) Lyme disease. <https://www.nhs.uk/conditions/lyme-disease/> Accessed 28.11.2017.

- NICE (2015). Lyme disease: testing. Clinical Knowledge Summary. Available at: <https://cks.nice.org.uk/lyme-disease#!diagnosissub:2>. Accessed 27 November 2017. (website not available in national archives)
- NICE (2016.) Lyme disease scoping consultation comments and responses
<https://www.nice.org.uk/guidance/indevelopment/gid-ng10007/documents>
- Nowotny, H., Scott, P.B., & Gibbons, M.T. (2001). *Re-Thinking Science: Knowledge and the Public in an Age of Uncertainty*. Policy Press, Cambridge.
- O'Connell, S. (1995). Lyme disease in the United Kingdom. *British Medical Journal* 310(6975), 303–8.
- O'Connor, S.M., Taylor, C.E., & Hughes, J.M. (2006). Emerging Infectious Determinants of Chronic Diseases. *Emerging Infectious Diseases* 12(7), 1051–1057.
- Orsini, M. & Smith, M. (2010). Social movements, knowledge and public policy: the case of autism activism in Canada and the US. *Critical Policy Studies*, 4(1): 38-57.
- Perronne, C. (2012). Lyme disease antiscience. *Lancet Infectious Diseases* 12(5), 361–362.
- PHE - Public Health England (undated) Lyme disease, ticks and your patient's health.
http://vscg.org/documents/uploads/PHE_Ticks_and_your_patients_health_leaflet_for_GPs.pdf.
Accessed 2/2/2017
- PHE - Public Health England (2014a). Suggested Referral Pathway for those patients with symptoms related to Lyme disease. At:
http://webarchive.nationalarchives.gov.uk/20140714085912/http://www.hpa.org.uk/webc/HPAwebbFile/HPAweb_C/1317141297288. Accessed 20.8.2018
- PHE - Public Health England (2014b). Lyme disease: diagnosis and treatment. Available at:
<https://www.gov.uk/government/publications/lyme-disease-diagnosis-and-treatment>. Accessed 15/3/19 (document noted 'withdrawn')

PHE - Public Health England (2015). Lyme Disease: Signs and Symptoms. Leaflet

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/718980/LymeDisease_SignsAndSymptoms_requested_changes_June_2018_final_Clean.pdf

PHE- Public Health England (2015, updated 2018). Lyme Disease: Signs and Symptoms. Available at:

<https://www.gov.uk/government/publications/lyme-disease-signs-and-symptoms>

PHE - Public Health England (2016). Re: Lyme disease testing. (Reply to FOI request) At:

https://www.whatdotheyknow.com/cy/request/313568/response/773785/attach/2/551%20FOI%20Lyme%20testing%20reply.pdf?cookie_passthrough=1. Accessed 14 August 2018.

Popay, J., & Williams, G. (1996) Public health research and lay knowledge. *Social Science & Medicine* 42(5): 759-768

Prior, L. (2008) Repositioning documents in social research. *Sociology* 42(5), 821-836.

Rabeharisoa V. (2003) The struggle against neuromuscular diseases in France and the emergence of the 'partnership model' of patient organisation. *Social Science & Medicine*. 2003, 2127–2136

Rabeharisoa, V., Moreira, T., & Akrich M. (2014). Evidence-based activism: Patients', users' and activists' groups in knowledge society. *Biosocieties* 9(2), 111-128.

Smith, K.E., & Stewart, E.A. (2017). Academic advocacy in public health: disciplinary 'duty' or political propaganda? *Social Science & Medicine* 189, 35-43.

Staley, K. & Doherty, C. (2016). It's not evidence, it's insight: bringing patients' perspectives into health technology appraisal at NICE. *Research Involvement and Engagement*, 2(1):
<https://doi.org/10.1186/s40900-016-0018-y>

Stiggelbout, A.M.T., Van der Weijden, M.P.T., De Wit, D., Frosch, F., Légaré, V.M., Montori, L., Treven, Elwyn, G. (2012). Shared decision making: really putting patients at the centre of healthcare. *British Medical Journal* 344, e256.

Stricker, R. B., & Johnson, L. (2008). Chronic Lyme disease and the “Axis of Evil”. *Future Microbiology*, 3(6), 621–624. At <http://www.futuremedicine.com/doi/pdf/10.2217/17460913.3.6.621>;

Tonks, A. (2007). Lyme wars. *British Medical Journal* 335(7626), 910–2.

Viramed Biotech AG (2015). Borrelia Virastrip IgG and IgM test kits. Document reference/name - 2297_Borrelia_ViraStripe_IgG_AL_RevB_en.doc
<http://www.viramed.de/en/bacteria/borrelia-species/borrelia-virastripe>; <https://www.invitech.co.uk>. Accessed 2/2/2017

VIRAS (2016) Submission to the NICE Lyme disease scoping consultation (2016)
<https://www.nice.org.uk/guidance/gid-ng10007/documents/consultation-comments-andresponses>. Accessed 2/2/2016

VIRAS (2017) Stakeholder comments on the NICE Draft Short Guideline November 6th, 2017
http://counsellingme.com/VIRAS/NICE/VIRAS_stakeholder_comment_summary3.pdf